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10/656,394	09/05/2003	Shaohong Qu	035718/268948	8698

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EXAMINER	
IBRAHIM, MEDINA AHMED	
ART UNIT	**PAPER NUMBER**
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/656,394	QU ET AL	
	Examiner	Art Unit	
	Medina A Ibrahim	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-21 are pending and are examined.

Sequence Listing

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and amino acid sequences set forth in 37 CFR1.821 (a)(1) and (a) (2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. The CRF and paper sequence listing of 09/05/03 have been entered. However, the sequence of Figure 5 has not been identified by SEQ ID NO: in the Brief Description of the Drawings on page 3 of the specification. Also, the sequences of Tables 1 and 4 on pages 36 and 41, respectively, have not been identified by SEQ ID NO: Applicant is respectfully requested to identify the sequences presented in the figure and the Tables 1 and 4 or to submit a new Sequence Listing which comprises said sequence.

Specification

The disclosure is objected to because of the following informalities: for example, page 20, line 4, of the specification contains an embedded hyperlink directed to an Internet address. The use of hyperlinks and/or other form of browser- executable code are not permitted under USPTO current policy because the content of such links are subject to a change, resulting in the introduction of New Matter into the specification. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 6, and 12 are indefinite for failing to recite specific hybridization and wash conditions for the claimed "stringent conditions". There are many different ways to define "stringent conditions". The specification provides exemplary conditions, but does not clearly describe the specific hybridization and wash conditions that define Applicant's "stringent". Hence, it is unknown what is encompassed by the claims. Appropriate correction to more clearly define the metes and bounds of the claims is required. Claims 2-5, 7-11, and 13-21 do not obviate the rejection, and therefore are included in the rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the construct designated as C2 comprising NB2, NBS3 and partial sequences of NBS1 and NBS4 and a method of inducing blast

disease resistance in a transgenic plant using said C2 construct, does not reasonably provide enablement for an isolated molecule that encodes a fragment of at least 40 contiguous amino acids of SEQ ID NO: 4, 8 or 12 having disease resistance activity, and nucleic acid molecule that hybridizes to SEQ ID NO: 3, 7 or 11 or nucleic acid molecule encoding SEQ ID NO: 4, 8 or 12 under stringent conditions, or the use of the isolated nucleic acid molecules encoding SEQ ID NO: 4, 8, or 12 to create or enhance disease resistance in a transgenic plant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims.

The claims are broadly drawn to an isolated nucleic acid molecule of SEQ ID NO: 3, 7 or 11 and a method of transforming plants with said nucleic acid to create or enhance disease resistance. The claims are also drawn to and nucleic acid molecule that hybridizes to SEQ ID NO: 3, 7 or 11 or a complement thereof; and to a nucleic acid molecule encoding SEQ ID NO: 4, 8 and 12 under any stringent conditions, wherein the nucleic acid molecule encodes a polypeptide having disease resistance activity; and a nucleic acid molecule encoding a fragment of at least 40 contiguous amino acid of SEQ ID NO: 4, 8, or 12, wherein the fragment retains disease resistance activity. The claims are also drawn to transgenic plant and plant cell stably transformed with a DNA construct comprising said nucleic acid molecule, and a method for enhancing or creating disease resistance in a plant with said nucleic acid molecules.

Applicant teaches high resolution mapping of the pi2 region using pi9 linked markers in F2 rice plants inoculated with a blast isolate and construction of a pi2 and

TAC library (Examples 1-2, pages 35-37). Applicant also teaches identification of NBS gene cluster of 99 kb contiguous sequence at the pi2 region (Examples 3-4, pages 37-38). Applicant further teaches isolation of six NBS-LRR genes designated as NBS1-6 in the pi2 sequence and the sequence comparison of said genes (pages 39-42, Examples 5-9). Applicant also teaches a construct comprising a 32 kb fragment containing NBS2, NBS3 and partial sequence of NBS1 and NBS4 and transformation of susceptible rice cultivars with said construct. Applicant teaches transformed rice plants with enhanced resistance against a blast disease as a result of coexpressing NBS2, NBS3 and partial sequence of NBS1 and NBS4 (Examples 14).

Applicant has not provided guidance for the disease resistance activity by SEQ ID NO: 3, 7 or 11 in a transgenic plant, much less of the nucleic acid molecules of claim 1, parts (c)-(e). Applicant has not taught a nucleic acid molecule that hybridizes to SEQ ID NO: 3, 7, and 11, to a complement thereof under any stringent conditions, wherein the nucleic acid molecule encodes a polypeptide having disease resistance activity. Applicant has not taught a nucleic acid molecule encoding a fragment of at least 40 contiguous amino acid of SEQ ID NO: 4, 8, or 12, wherein the fragment retains disease resistance activity. Applicant has not provided guidance for the production of transgenic plant having resistance against all diseases including all fungi, nematodes, bacteria, insects, and virus using exemplified or non-exemplified nucleic acid molecules. The scope of the nucleic acid molecules of the claims encompasses nucleic acid molecules with multiple modifications including multiple deletions and/or substitutions that retain the ability to encode a polypeptide with disease resistance activity. However, Applicant

has provided no guidance for any modifications to SEQ ID NO: 3, 7, and11 that resulted in nucleic acid molecules having both the structural and functional properties as recited in the claims. In addition, no transgenic plant having resistance against exemplified or non-exemplified pathogen as a result of expressing said nucleic acid variants has been disclosed.

While mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims. One skilled in the art would expect any tolerance to modification for a given DNA/protein to diminish with each further and additional modification or multiple substitutions/ deletions. One skilled in the art would have to make all possible nucleotide substitutions and deletions in the 3000 nucleotide long sequence of SEQ ID NO: 3, 7 or 11 and test all nucleotide sequences that meets the structural limitations to determine which also meet the functional limitation. One would also have to test and evaluate disease resistance activity of the nucleic acid molecules as broadly in a transgenic plant.

The only working example disclosed in the specification fails to provide disease resistance activity by SEQ ID NO: 3, 7, or 11, separately. Example 14 of the specification teaches transformation of susceptible rice plants with a construct containing NBS2 and NBS3 and partial sequence of NBS1 and NBS4. However, the detected resistant phenotype in the transgenic rice plants could be the function of all four genes or gene fragments of two or more. It may be also that the expression of all four genes or the pi2 gene cluster is essential for blast resistance activity in susceptible plants. Therefore, based upon Applicant's working example, it is unpredictable as to

whether the expression of SEQ ID NO: 3, 7, or 11 would create or enhance disease resistance in a plant.

In *Genentech Inc* v. *Novo Nordisk A/S* (42 USPQ2d 1001 at p. 1005) the court stated "(p)atent protection is granted in return for an enabling disclosure of an invention, not for vague intimidations of general ideas that may or may not workable.... When there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required....". Applicant is here expecting others to determine how to use individual disclosed nucleic acid molecules including modified and unmodified sequences in a transgenic plant to create or enhance resistance against plant pathogens.

Therefore, given the breadth of the claims, the unpredictability in the art with respect to DNA/protein modifications, the limited guidance and working examples in the specification as discussed supra, and the state of the prior art, the claimed invention is not enabled throughout the broad scope. See In re Wands 858 F.2d 731, 8USPQ2nd 1400 (Fed. Cir, 1988).

See, also, *Amgen Inc. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at 1027 (Fed. Cir. 1991) where the court held that the disclosure of a few gene sequences did not enable claims broadly drawn to any analog thereof.

Written Description

Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention.

The claims are broadly drawn to an isolated nucleic acid molecule that hybridizes to SEQ ID NO: 3, 7, and 11, to a complement thereof; and to a nucleic acid molecule encoding SEQ ID NO: 4, 8 and 12 under any stringent conditions, wherein the nucleic acid molecule encodes a polypeptide having disease resistance activity; and a nucleic acid molecule encoding a fragment of at least 40 contiguous amino acid of SEQ ID NO: 4, 8, or 12, wherein the fragment retains disease resistance activity. The claims are also drawn to transgenic plant and plant cell stably transformed with a DNA construct comprising said nucleic acid molecule, and a method for enhancing or creating disease resistance in a plant with said nucleic acid molecules. In contrast, Applicant describes the nucleic acid molecules of SEQ ID NO: 3, 7, and 11 encoding SEQ ID NO: 4, 8 and 12, transgenic plant, plant cell, vector, and DNA construct comprising said nucleic acid molecules. These are genus claims.

In *Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), the court stated:

> An adequate written description of a DNA "requires a precise definition, such as by structure, formula, chemical name, or physical properties", not a mere wish or plan for obtaining the claimed chemical invention... Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it; what is required is a description of the DNA itself (43 USPQ2d at 1404).

The court held that held that human insulin-encoding cDNA is not described by prophetic example, which sets forth only a general method for obtaining the human cDNA:

> The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity... Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes...does not necessarily describe the DNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA....Accordingly,

the specification does not provide a written description of human cDNA (43 USPQ2d at 1405).

The description of a single species of rat cDNA was held insufficient to describe the broad genera of vertebrate or mammalian insulin:

"In claims to genetic material...a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It doesn't define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function...does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is (43 USPQ2d at 1406).

The court continued:

"Thus...a cDNA is not defined by the mere name 'cDNA', even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA...A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus". (43 USPQ2d at 1406). See also where the court teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from the organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

Applicant has not described the composition and structure of all nucleic acid molecules encompassed by the claims. One would not expect that the majority of the nucleic acid molecules that hybridize to SEQ ID NO: 3, 7, or 11 under any stringency conditions would encode a polypeptide having the activity of SEQ ID NO: 4, 8 or 12. The hybridizing sequences are expected to vary because " stringent conditions" (is open to individual interpretations) will yield unrelated nucleic acid molecules. Therefore,

a substantial variation in structures and function is expected among the claimed nucleic acid molecules. Applicant has not described a representative number of nucleic acids encoding polypeptides that share 40 contiguous amino acids. Therefore, the disclosure of SEQ ID NO: 3, 7, and 11 (and few genes from rice described in the specification) is not a representative species of the genus of the claims. Therefore, the specification fails to adequately describe the nucleotide sequences as broadly claimed. Consequently, the specification has not provided an adequate description for DNA constructs, vectors, plant cells and plants comprising said nucleic acid molecules. Given this lack of description of representative nucleic acid molecules encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that Applicant was in possession of the invention as broadly claimed at the time of filing.

Therefore, weighing all factors above, the claimed invention does not meet the current written description requirements.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 and 8-12, 14-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Yano et al (US 6, 274, 789 (A)).

The claims are broadly drawn to an isolated nucleic acid molecule that hybridizes

to SEQ ID NO: 3, 7, and 11, to a complement thereof; and to a nucleic acid molecule encoding SEQ ID NO: 4, 8 and 12 under any stringent conditions, wherein the nucleic acid molecule encodes a polypeptide having disease resistance activity; a DNA construct and vector comprising said nucleic acid molecule operably linked to a promoter, transgenic plant / cell/seed stably transformed with a DNA construct and a method of transforming a plant with said DNA construct. The claims are also drawn to specific monocot plants including barley, rice and maize. The "stringency conditions" is not clearly defined in the specification (see 112,2nd rejection above).

Yano et al teaches an isolated DNA from rice encoding a polypeptide resistance to a broad range of rice blast fungi, a vector or DNA construct comprising said isolated DNA operably linked to a constitutive or inducible promoter, and a method for transforming and regenerating plants from transformed plant cells expressing said isolated DNA. The cited reference also teaches transformed plants and plant cells and seed including rice, wheat and barley with resistance to blast disease (columns 1-2, 6-7, 9-10, and 39-40). Given the broad interpretation of "stringent conditions" the DNA sequences disclosed by Yano et al would inherently hybridize to Applicant's nucleic acid molecule of claim 1, absent evidence to the contrary. Therefore, Yano et al disclose all claim limitations.

Claims 1-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Hodges et al (US 5, 677, 175 (B)).

Hodges et al teaches an isolated DNA from rice encoding a polypeptide resistance to rice blast fungi, a vector or DNA construct comprising said isolated DNA

operably linked to a constitutive or inducible promoter, and a method for transforming and regenerating plants from transformed plant cells expressing said isolated DNA. The cited reference also teaches transformed plants and plant cells and seed including rice, tobacco and potato with resistance to fungal diseases (columns 1-8 and 13-14). Given the broad interpretation of "stringent conditions" the DNA sequences disclosed by Hodges et al would inherently hybridize to Applicant's nucleic acid molecule of claim 1 , absent evidence to the contrary. Therefore, Hodges et al disclose all claim limitations.

Remarks

No claim is allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is (571) 272-0797. The Examiner can normally be reached Monday -Thursday from 8:00AM to 5:30PM and every other Friday from 9:00AM to 5:00 PM . Before and after final responses should be directed to fax nos. (703) 872-9306 and (703) 872-9307, respectively.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Amy Nelson, can be reached at (571) 272-0804.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

3/4/05
Mai

Medina A. Ibrahim

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PATENT EXAMINER